

## COMPLETE THE STN SURVEY - APRIL 27 THROUGH MAY 31

Dear valued STN customer,

In an effort to enhance your experience with STN, we would like to better understand what you find useful. Please take approximately 5 minutes to complete a web survey.

If you provide us with your name, login ID, and e-mail address, you will be entered in a drawing to win a free iPod(R). Your responses will be kept confidential and will help us make future improvements to STN.

Take survey: <http://www.zoomerang.com/survey.zgi?p=WEB2259HNKWTUW>

Thank you in advance for your participation.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 16:25:17 ON 18 MAY 2006

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 16:25:29 ON 18 MAY 2006

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STRUCTURE FILE UPDATES: 17 MAY 2006 HIGHEST RN 884739-24-6

DICTIONARY FILE UPDATES: 17 MAY 2006 HIGHEST RN 884739-24-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
 \*  
 \* The CA roles and document type information have been removed from \*  
 \* the IDE default display format and the ED field has been added, \*  
 \* effective March 20, 2005. A new display format, IDERL, is now \*  
 \* available and contains the CA role and document type information. \*  
 \*  
 \*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of

10/532,397

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptal20ltxs

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 JAN 17 Pre-1988 INPI data added to MARPAT  
NEWS 4 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist  
visualization results  
NEWS 5 FEB 22 The IPC thesaurus added to additional patent databases on STN  
NEWS 6 FEB 22 Updates in EPFULL; IPC 8 enhancements added  
NEWS 7 FEB 27 New STN AnaVist pricing effective March 1, 2006  
NEWS 8 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes  
NEWS 9 MAR 22 EMBASE is now updated on a daily basis  
NEWS 10 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL  
NEWS 11 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC  
thesaurus added in PCTFULL  
NEWS 12 APR 04 STN AnaVist \$500 visualization usage credit offered  
NEWS 13 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced  
NEWS 14 APR 12 Improved structure highlighting in FQHIT and QHIT display  
in MARPAT  
NEWS 15 APR 12 Derwent World Patents Index to be reloaded and enhanced during  
second quarter; strategies may be affected  
NEWS 16 MAY 10 CA/CAPLUS enhanced with 1900-1906 U.S. patent records  
NEWS 17 MAY 11 KOREAPAT updates resume  
  
NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.  
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT  
<http://download.cas.org/express/v8.0-Discover/>  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8  
NEWS X25 X.25 communication option no longer available after June 2006

Enter NEWS followed by the item number or name to see news on that  
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\* \* \* \* \*

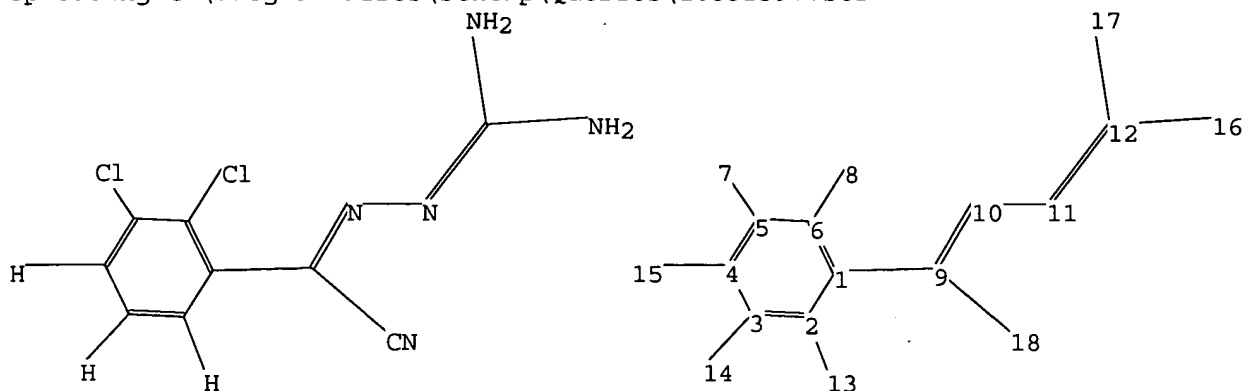
10/532,397

experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10532397.str



chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6

chain bonds :

1-9 2-13 3-14 4-15 5-7 6-8 9-10 9-18 10-11 11-12 12-16 12-17

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

9-10 10-11 11-12 12-16 12-17

exact bonds :

1-9 2-13 3-14 4-15 5-7 6-8 9-18

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS  
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> s 11

SAMPLE SEARCH INITIATED 16:25:45 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

10/532,397

BATCH      \*\*COMPLETE\*\*  
PROJECTED ITERATIONS:      0 TO      0  
PROJECTED ANSWERS:      0 TO      0

L2      0 SEA SSS SAM L1

=> s l1 ful  
FULL SEARCH INITIATED 16:25:53 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED -      13 TO ITERATE

100.0% PROCESSED      13 ITERATIONS      4 ANSWERS  
SEARCH TIME: 00.00.01

L3      4 SEA SSS FUL L1

=> file caplus  
COST IN U.S. DOLLARS      SINCE FILE      TOTAL  
ENTRY      SESSION  
FULL ESTIMATED COST      197.70      197.91

FILE 'CAPLUS' ENTERED AT 16:29:10 ON 18 MAY 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE COVERS 1907 - 18 May 2006 VOL 144 ISS 21  
FILE LAST UPDATED: 17 May 2006 (20060517/ED)

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<http://www.cas.org/infopolicy.html>

=> s l3  
L5      13 L3

=> s l5 and (prcess or prepar? or synthet? or method or make or made)  
8 PRCESS  
3 PRCESSES  
11 PRCESS  
    (PRCESS OR PRCESSES)  
1642623 PREPAR?  
122308 PREP  
2152 PREPS  
124251 PREP  
    (PREP OR PREPS)  
2004324 PREPD

10/532,397

17 PREPDS  
2004336 PREPD  
(PREPD OR PREPDS)  
120593 PREPG  
12 PREPGS  
120604 PREPG  
(PREPG OR PREPGS)  
2706376 PREPN  
204232 PREPNS  
2860453 PREPN  
(PREPN OR PREPNS)  
4733151 PREPAR?  
(PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)  
643031 SYNTHET?  
3087757 METHOD  
1267044 METHODS  
3997894 METHOD  
(METHOD OR METHODS)  
230642 MAKE  
179438 MAKES  
397753 MAKE  
(MAKE OR MAKES)  
1204221 MADE  
25 MADES  
1204242 MADE  
(MADE OR MADES)

L6 13 L5 AND (PRCESS OR PREPAR? OR SYNTHET? OR METHOD OR MAKE OR MADE)

=> s l6 and (methanesulphonic or methanesulfornic or methanesulfonic)

6 METHANESULPHONIC  
0 METHANESULFORNIC  
8675 METHANESULFONIC

L7 2 L6 AND (METHANESULPHONIC OR METHANESULFORNIC OR METHANESULFONIC)

=> d l7 ibib hitstr abs 1-2

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:390214 CAPLUS

DOCUMENT NUMBER: 140:391299

TITLE: Process for **preparing** 2-(2,3-dichlorophenyl)-  
2-(aminoguanidine)acetonitrile and a process for its  
cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-  
1,2,4-triazine

INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi

PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

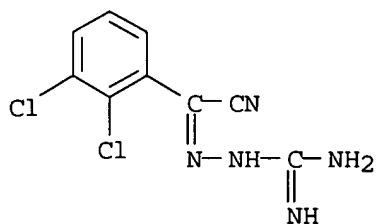
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

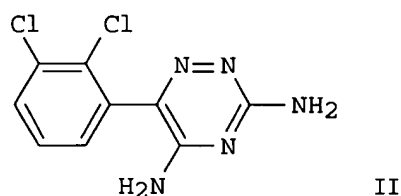
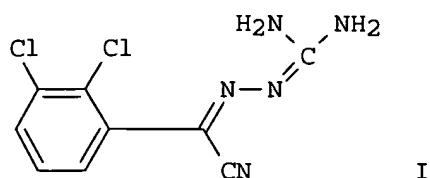
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,				

OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,  
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 ES 2209639 A1 20040616 ES 2002-2502 20021031  
 ES 2209639 B1 20050801  
 AU 2003272019 A1 20040525 AU 2003-272019 20031027  
 EP 1556341 A1 20050727 EP 2003-753860 20031027  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 US 2006052625 A1 20060309 US 2005-532397 20050422  
 NO 2005002574 A 20050527 NO 2005-2574 20050527  
 PRIORITY APPLN. INFO.: ES 2002-2502 A 20021031  
 WO 2003-IB4763 W 20031027  
 OTHER SOURCE(S): CASREACT 140:391299  
 IT **84689-20-3P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (process for **preparing** 2-(2,3-dichlorophenyl)-2-  
 (aminoguanidine)acetonitrile and a process for its cyclization into  
 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)  
 RN 84689-20-3 CAPLUS  
 CN Hydrazinecarboximidamide, 2-[cyano(2,3-dichlorophenyl)methylene] - (9CI)  
 (CA INDEX NAME)



GI



AB A method for preparing the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with aminoguanidine bicarbonate in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an alyph alc. (e.g., ethanol) or alc.-water mixture

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267313 CAPLUS

DOCUMENT NUMBER: 140:303705

TITLE: Two-step process for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate

INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

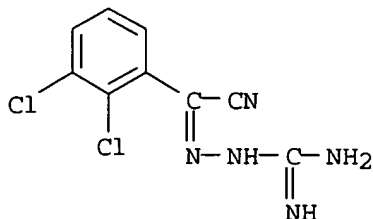
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,				

9/18/03

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 CA 2498761 AA 20040401 CA 2003-2498761 20030918  
 AU 2003267676 A1 20040408 AU 2003-267676 20030918  
 EP 1539720 A1 20050615 EP 2003-748368 20030918  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 PRIORITY APPLN. INFO.: HU 2002-3114 A 20020920  
 WO 2003-HU72 W 20030918  
 OTHER SOURCE(S): CASREACT 140:303705  
 IT **84689-20-3P**  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (in a two-step process for the synthesis of high-purity  
 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from  
 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate)  
 RN 84689-20-3 CAPLUS  
 CN Hydrazinecarboximidamide, 2-[cyano(2,3-dichlorophenyl)methylene] - (9CI)  
 (CA INDEX NAME)



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is **prepared** by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of **methanesulfonic** acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y  
 COST IN U.S. DOLLARS

SINCE FILE TOTAL  
 ENTRY SESSION



10/532,397

FULL ESTIMATED COST	31.45	229.36
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.50	-1.50

STN INTERNATIONAL LOGOFF AT 16:34:06 ON 18 MAY 2006

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Welcome to STN International! Enter x:x

LOGINID:sssptal201txs

PASSWORD:

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\* \* \* \* \* Welcome to STN International \* \* \* \* \*

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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 17	Pre-1988 INPI data added to MARPAT
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NEWS 16	MAY 10	CA/CAPLUS enhanced with 1900-1906 U.S. patent records
NEWS 17	MAY 11	KOREAPAT updates resume
NEWS EXPRESS		FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005. V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT <a href="http://download.cas.org/express/v8.0-Discover/">http://download.cas.org/express/v8.0-Discover/</a>
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS LOGIN		Welcome Banner and News Items
NEWS IPC8		For general information regarding STN implementation of IPC 8
NEWS X25		X.25 communication option no longer available after June 2006

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In an effort to enhance your experience with STN, we would like to better understand what you find useful. Please take approximately 5 minutes to complete a web survey.

If you provide us with your name, login ID, and e-mail address, you will be entered in a drawing to win a free iPod(R). Your responses will be kept confidential and will help us make future improvements to STN.

Take survey: <http://www.zoomerang.com/survey.zgi?p=WEB2259HNKWTUW>

Thank you in advance for your participation.

\*\*\*\*\* STN Columbus \*\*\*\*\*

FILE 'HOME' ENTERED AT 16:38:15 ON 18 MAY 2006

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 16:38:22 ON 18 MAY 2006

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STRUCTURE FILE UPDATES: 17 MAY 2006 HIGHEST RN 884739-24-6

DICTIONARY FILE UPDATES: 17 MAY 2006 HIGHEST RN 884739-24-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*

\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*

10/532,397

\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

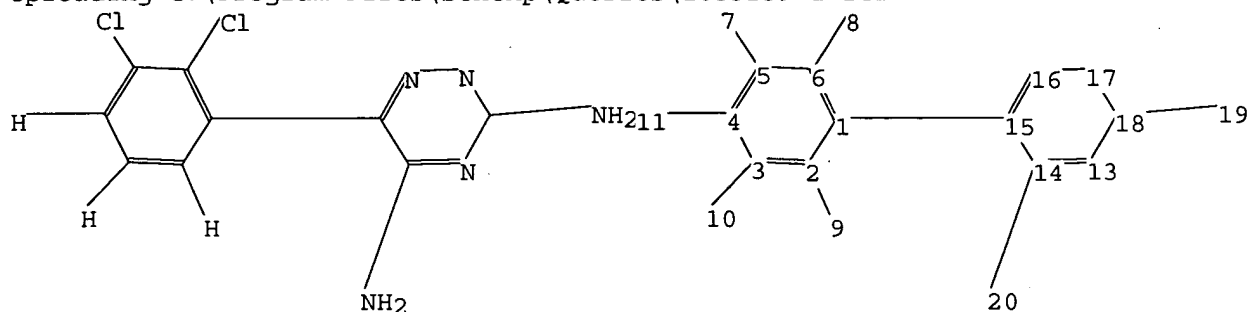
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\105323971.str



chain nodes :

7 8 9 10 11 19 20

ring nodes :

1 2 3 4 5 6 13 14 15 16 17 18

chain bonds :

1-15 2-9 3-10 4-11 5-7 6-8 14-20 18-19

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 13-14 13-18 14-15 15-16 16-17 17-18

exact/norm bonds :

13-14 13-18 14-15 14-20 15-16 16-17 17-18 18-19

exact bonds :

1-15 2-9 3-10 4-11 5-7 6-8

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 : 13 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS  
11:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS

L1 STRUCTURE UPLOADED

=> s 11

10/532,397

SAMPLE SEARCH INITIATED 16:38:40 FILE 'REGISTRY'  
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100.0% PROCESSED 6 ITERATIONS 3 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
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PROJECTED ANSWERS: 3 TO 163

L2 3 SEA SSS SAM L1

=> s 11 ful  
FULL SEARCH INITIATED 16:38:47 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 139 TO ITERATE

100.0% PROCESSED 139 ITERATIONS 50 ANSWERS  
SEARCH TIME: 00.00.01

L3 50 SEA SSS FUL L1

=> file caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 166.94 167.15

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FILE LAST UPDATED: 17 May 2006 (20060517/ED)

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=> s 13  
L4 1097 L3

=> s 14 and (process or prepar? or synthet? or method or made or make)  
2243839 PROCESS  
1517987 PROCESSES  
3347670 PROCESS  
(PROCESS OR PROCESSES)

10/532,397

1642623 PREPAR?  
122308 PREP  
2152 PREPS  
124251 PREP  
(PREP OR PREPS)  
2004324 PREPD  
17 PREPDS  
2004336 PREPD  
(PREPD OR PREPDS)  
120593 PREPG  
12 PREPGS  
120604 PREPG  
(PREPG OR PREPGS)  
2706376 PREPN  
204232 PREPNS  
2860453 PREPN  
(PREPN OR PREPNS)  
4733151 PREPAR?  
(PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)  
643031 SYNTHET?  
3087757 METHOD  
1267044 METHODS  
3997894 METHOD  
(METHOD OR METHODS)  
1204221 MADE  
25 MADES  
1204242 MADE  
(MADE OR MADES)  
230642 MAKE  
179438 MAKES  
397753 MAKE  
(MAKE OR MAKES)  
L5 469 L4 AND (PROCESS OR PREPAR? OR SYNTHET? OR METHOD OR MADE OR  
MAKE)

=> s 15 and aminoguanidine bicarbonate

4393 AMINO GUANIDINE  
179 AMINO GUANIDINES  
4466 AMINO GUANIDINE  
(AMINO GUANIDINE OR AMINO GUANIDINES)  
49464 BICARBONATE  
8106 BICARBONATES  
55312 BICARBONATE  
(BICARBONATE OR BICARBONATES)  
328 AMINO GUANIDINE BICARBONATE  
(AMINO GUANIDINE(W) BICARBONATE)

L6 9 L5 AND AMINO GUANIDINE BICARBONATE

=> s 16 and (methanesulphonic or mthanesulfornic or methanesulfonic)

6 METHANESULPHONIC  
0 MTHANESULFORNIC  
8675 METHANESULFONIC

L7 2 L6 AND (METHANESULPHONIC OR MTHANESULFORNIC OR METHANESULFONIC)

=> d 16 ibib hitstr abs 1-9

L6 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:421792 CAPLUS  
DOCUMENT NUMBER: 142:430313

TITLE: **Process for preparation of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (Lamotrigine) via reaction of 2,3-dichlorobenzoyl chloride with cuprous cyanide and then with aminoguanidine bicarbonate followed by cyclization.**

INVENTOR(S): Vyas, Sharad Kumar

PATENT ASSIGNEE(S): Torrent Pharmaceuticals Ltd., India

SOURCE: Indian, 12 pp.  
CODEN: INXXAP

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 183150	A	19990925	IN 1998-CA2171	19981214
AT 250041	E	20031015	AT 1999-956293	19991207
RU 2231526	C2	20040627	RU 2001-115698	19991207
PRIORITY APPLN. INFO.:			IN 1998-CA2171	A 19981214
			WO 1999-IB1955	W 19991207

OTHER SOURCE(S): CASREACT 142:430313

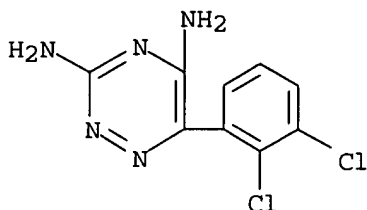
IT **84057-84-1P**, Lamotrigine

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(**preparation** of lamotrigine via reaction of dichlorobenzoyl chloride with cuprous cyanide and then with **aminoguanidine bicarbonate** followed by cyclization)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



AB Lamotrigine was **prepared** by reaction of 2,3-dichlorobenzoyl chloride with CuCN (1:1-2 molar ratio) in MeCN and a cosolvent to produce dichlorobenzoyl cyanide, reaction of the latter with **aminoguanidine bicarbonate** to produce the cyanoimine intermediate 2-[cyano(2,3-dichlorophenyl)methylene]hydrazinecarboximidamide, and cyclization of this in the presence of aqueous KOH at 80°-reflux.

L6 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:421470 CAPLUS

DOCUMENT NUMBER: 141:7119

TITLE: **Preparation of crystalline lamotrigine and its monohydrate**

INVENTOR(S): Manjunatha, Sulur G.; Kulkarni, Ashok Krishna; Kishore, Charugundia; Bokka, Ravisankar

PATENT ASSIGNEE(S): Jubilant Organosys Limited, India

SOURCE: Brit. UK Pat. Appl., 25 pp.

CODEN: BAXXDU  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2395483	A1	20040526	GB 2003-15608	20030703
WO 2005003104	A2	20050113	WO 2004-IN186	20040628
WO 2005003104	A3	20050922		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2003-15608 A 20030703

OTHER SOURCE(S): CASREACT 141:7119

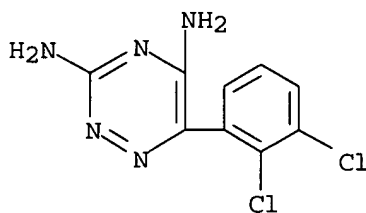
IT **84057-84-1P**, Lamotrigine **375347-20-9P**, Lamotrigine monohydrate

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(X-ray diffraction anal.; **preparation** of crystalline lamotrigine and its monohydrate by condensation of 2,3-dichlorobenzoyl cyanide with aminoguanidine and cyclization)

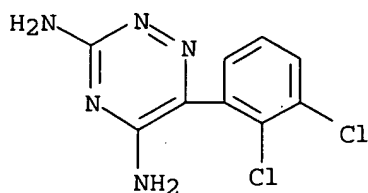
RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)

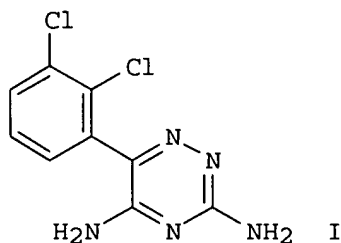


RN 375347-20-9 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrate (9CI) (CA INDEX NAME)

● H<sub>2</sub>O

GI



AB The invention relates to crystalline lamotrigine (3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine) (I) monohydrate and anhydrous lamotrigine. An improved **process** for manufacturing these products comprises reacting 2,3-dichlorobenzoyl cyanide with **aminoguanidine bicarbonate** in aqueous mineral acid, optionally together with a water miscible organic solvent, at 30-80° to produce the 2-(2,3-dichlorophenyl)-2-(guanidinylimino)acetonitrile (Schiff base) (II). The Schiff base II is further cyclized in aqueous organic solvent, e.g. alc. to produce pure lamotrigine of a pharmaceutically acceptable quality which on further drying at 45-50° under vacuum yields lamotrigine monohydrate, and/or on further drying at 100-110° yields anhydrous lamotrigine. The lamotrigine monohydrate or anhydrous lamotrigine thereby produced may then be brought into association with a pharmaceutically acceptable carrier for administration to a patient in need thereof.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:390214 CAPLUS

DOCUMENT NUMBER: 140:391299

TITLE: **Process for preparing**  
2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile  
and a **process** for its cyclization into  
3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine

INVENTOR(S): Dalmases Barjoan, Pere; Bessa Bellmunt, Jordi

PATENT ASSIGNEE(S): Laboratorios Vita, S.A., Spain

SOURCE: PCT Int. Appl., 17 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English



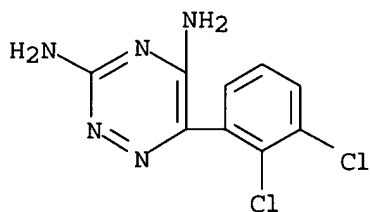
10/532,397

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

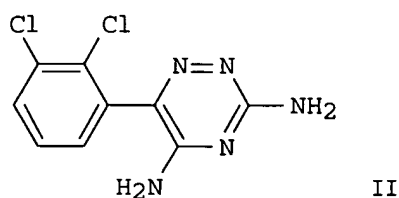
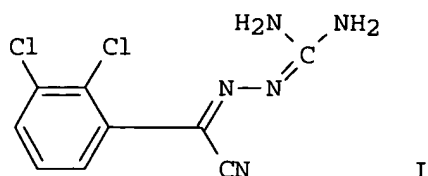
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039767	A1	20040513	WO 2003-IB4763	20031027
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
ES 2209639	A1	20040616	ES 2002-2502	20021031
ES 2209639	B1	20050801		
AU 2003272019	A1	20040525	AU 2003-272019	20031027
EP 1556341	A1	20050727	EP 2003-753860	20031027
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2006052625	A1	20060309	US 2005-532397	20050422
NO 2005002574	A	20050527	NO 2005-2574	20050527
PRIORITY APPLN. INFO.:			ES 2002-2502	A 20021031
			WO 2003-IB4763	W 20031027

OTHER SOURCE(S): CASREACT 140:391299

IT **84057-84-1P**, 3,5-Diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (**process** for **preparing** 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile and a **process** for its cyclization into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine)  
 RN 84057-84-1 CAPLUS  
 CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



GI



AB A **method** for **preparing** the intermediate 2-(2,3-dichlorophenyl)-2-(aminoguanidine)acetonitrile (I; m.p. 180-183°) which comprises the condensation reaction of 2,3-dichlorobenzoyl cyanide with **aminoguanidine bicarbonate** in a non-aqueous medium in the presence of methanesulfonic acid, which produces good I yields and short reaction times. I is cyclized into 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (II; m.p. 217°) under reflux in an aliph. alc. (e.g., ethanol) or alc.-water mixture

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:267313 CAPLUS

DOCUMENT NUMBER: 140:303705

TITLE: Two-step **process** for the synthesis of high-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate

INVENTOR(S): Neu, Jozsef; Gizur, Tibor; Toerley, Jozsef; Csabai, Janos; Vegh, Ferenc; Kalvin, Peter; Tarkanyi, Gabor

PATENT ASSIGNEE(S): Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

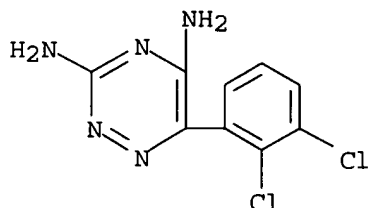
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026845	A1	20040401	WO 2003-HU72	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
 PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,  
 TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 CA 2498761 AA 20040401 CA 2003-2498761 20030918  
 AU 2003267676 A1 20040408 AU 2003-267676 20030918  
 EP 1539720 A1 20050615 EP 2003-748368 20030918  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 PRIORITY APPLN. INFO.: HU 2002-3114 A 20020920  
 WO 2003-HU72 W 20030918  
 OTHER SOURCE(S): CASREACT 140:303705  
 IT **84057-84-1P**, Lamotrigine  
 RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP  
 (Preparation)  
 (two-step **process** for the synthesis of high-purity  
 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine from  
 2,3-dichlorobenzoyl cyanide and aminoguanidine dimesylate)  
 RN 84057-84-1 CAPLUS  
 CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB High-purity 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (I; i.e., lamotrigine) is **prepared** by the condensation reaction of 2,3-dichlorobenzoyl cyanide (II) with 1-2 mol equivalent of an aminoguanidine salt (e.g., aminoguanidine dimesylate) in 3-6 mol equivalent of methanesulfonic acid, then the obtained adduct (III) is transformed without isolation into the desired product by contacting it with magnesium oxide, followed by crystallization of the product from an appropriate organic solvent (e.g., acetone).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:76761 CAPLUS  
 DOCUMENT NUMBER: 138:137336  
 TITLE: **Method** for producing lamotrigine from

alpha-oxo-2,3-dichlorophenylacetamidinoaminoguanidino  
hydrazone by ring closure reaction

INVENTOR(S): Schneider, Geza; Gegoe, Csaba Lehel; Ondi, Levente;  
Mate, Attila Gergely; Lukacs, Ferenc; Nyerges, Miklos;  
Garaczi, Sandor

PATENT ASSIGNEE(S): Helm AG, Germany; CF Pharma Gyogyszergyarto Kft.

SOURCE: PCT Int. Appl., 21 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

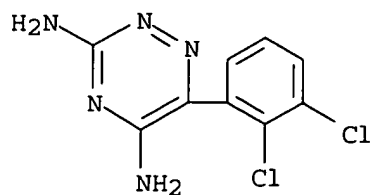
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008393	A1	20030130	WO 2002-EP7433	20020704
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10134980	A1	20030213	DE 2001-10134980	20010717
DE 10134980	C2	20030528		
EP 1311492	A1	20030521	EP 2002-758308	20020704
EP 1311492	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE				
CA 2417435	C	20040113	CA 2002-2417435	20020704
CA 2417435	AA	20030130		
ES 2224074	T3	20050301	ES 2002-2758308	20020704
US 2003191310	A1	20031009	US 2003-343225	20030515
US 6683182	B2	20040127		
PRIORITY APPLN. INFO.:			DE 2001-10134980	A 20010717
			WO 2002-EP7433	W 20020704
OTHER SOURCE(S): CASREACT 138:137336; MARPAT 138:137336				
IT 493025-05-1P, Lamotrigine hydrochloride				
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of lamotrigine from $\alpha$ -oxo-2,3- dichlorophenylacetamidinoaminoguanidino hydrazone by a ring closure reaction)				
RN 493025-05-1 CAPLUS				
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)-, monohydrochloride (9CI) (CA INDEX NAME)				

10/532,397



● HCl

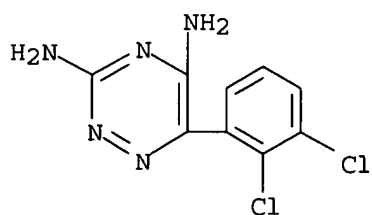
IT 84057-84-1P, Lamotrigine

RL: SPN (Synthetic preparation); PREP (Preparation)

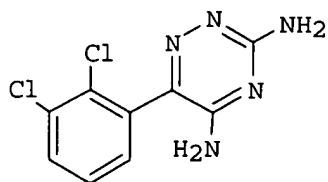
(preparation of lamotrigine from  $\alpha$ -oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone by a ring closure reaction)

RN 84057-84-1 CAPLUS

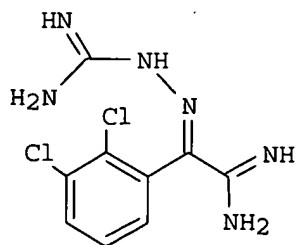
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



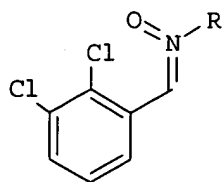
GI



I



II



III

AB The invention relates to a **method** for producing 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine [lamotrigine (I)], or its pharmaceutically acceptable salts, by ring closure reaction from  $\alpha$ -oxo-2,3-dichlorophenylacetamidinoaminoguanidino hydrazone (II) or its salts. The **preparation** of II from N-oxides, III [R = linear, branched or cyclic (un)substituted alkyl, aryl, aralkyl], or their salts, are also described. Thus, I was **prepared** from 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH:N(O)Ph, via cyanation with NaCN, amination to the acetamidine hydrochloride, reaction with aminoguanine bicarbonate to give II·HCl, treatment with aqueous NaOH to give the free base, which is cyclized to I; cyclization of II·HCl gives I·HCl.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:631908 CAPLUS

DOCUMENT NUMBER: 135:195578

TITLE: **Process for preparing** substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines

INVENTOR(S): Nadaka, Vladimir; Lexner, Jael; Kaspi, Joseph

PATENT ASSIGNEE(S): Chemagis Ltd., Israel

SOURCE: Eur. Pat. Appl., 9 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1127873	A2	20010829	EP 2001-103660	20010223
EP 1127873	A3	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IL 134730	A1	20031031	IL 2000-134730	20000225
CA 2337280	AA	20010825	CA 2001-2337280	20010215
US 2001025118	A1	20010927	US 2001-789634	20010222
US 6329521	B2	20011211		

PRIORITY APPLN. INFO.: IL 2000-134730 A 20000225

OTHER SOURCE(S): CASREACT 135:195578; MARPAT 135:195578

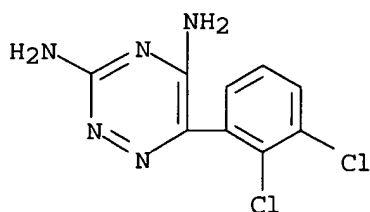
IT **84057-84-1P**

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

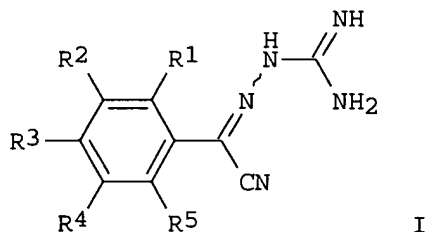
(**process for preparing** substituted benzoyl cyanide amidinohydrazones as intermediates for synthesis of 3,5-diamino-6-phenyl-1,2,4-triazines)

RN 84057-84-1 CAPLUS

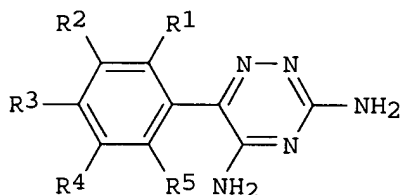
CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



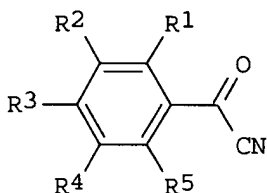
GI



I



II



III

AB The title compds. [I; R1-R5 = H, halo, alkyl, etc.], useful as intermediates for synthesis of 1,2,4-triazines II (active in the treatment of CNS disorders), were **prepared** by reacting the benzoyl cyanides III with **aminoguanidine bicarbonate** in a mixture of a water-soluble solvent and polyphosphoric acid. Thus, reacting 2,3-dichlorobenzoyl cyanide with **aminoguanidine bicarbonate** in the presence of polyphosphoric acid in MeCN afforded 2,3-dichlorobenzoyl cyanide amidinohydrazone which was then heated under reflux in ProH to give 2,3-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine.

L6 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:507682 CAPLUS

DOCUMENT NUMBER: 135:108912

TITLE: **Preparation of 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (lamotrigine)**

INVENTOR(S): Radhakrishnan, Tarur Venkatasubramanian; Sasikumar, Thoovara Mohan; Srivastava, Anita Ranjan

PATENT ASSIGNEE(S): RPG Life Sciences Limited, India

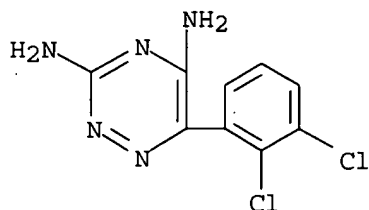
SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049669	A1	20010712	WO 2000-IN1	20000103
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2372988	A1	20020911	GB 2002-14791	20000103
GB 2372988	B2	20040407		
BR 2000016980	A	20021001	BR 2000-16980	20000103
DE 10085384	T	20021212	DE 2000-10085384	20000103
AU 763244	B2	20030717	AU 2000-44288	20000103
US 6639072	B1	20031028	US 2002-149429	20020624
PRIORITY APPLN. INFO.:			WO 2000-IN1	A 20000103
IT	84057-84-1P, Lamotrigine			
	RL: IMF (Industrial manufacture); PREP (Preparation) (preparation of)			
RN	84057-84-1 CAPLUS			
CN	1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)			



AB The title compound was **prepared** by hydrogenation of 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>NO<sub>2</sub> in MeOH at 80 psi H pressure using Raney Ni catalyst at 30° to give 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>NH<sub>2</sub> which was diazotized and converted to nitrile with CuCN/NaCN at 65-70°. The resulting 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CN was hydrolyzed to give 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub> which was converted to acid chloride at 80° with SOCl<sub>2</sub>. The 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>COCl was cyano-dehalogenated with CuCN/KI by refluxing in PhCl under an inert atmospheric and the product 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>COCN was condensed with **aminoguanidine bicarbonate** in PhMe in the presence of H<sub>2</sub>SO<sub>4</sub> and p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H at 100-120°, followed by in-situ cyclization of the Schiff base by refluxing with MeONa in MeOH. Crude lamotrigine is purified by recrystn. from MeOH.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:112505 CAPLUS

DOCUMENT NUMBER: 108:112505

TITLE: **Preparation** of 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine isethionate as an



antiepileptic  
 INVENTOR(S): Sawyer, David Alan; Copp, Frederick Charles  
 PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK  
 SOURCE: Eur. Pat. Appl., 5 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

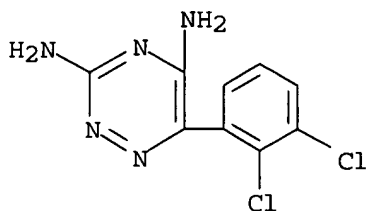
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 247892	A1	19871202	EP 1987-304776	19870529
EP 247892	B1	19910424		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8702759	A	19871201	DK 1987-2759	19870529
DK 166278	B	19930329		
DK 166278	C	19930823		
FI 8702406	A	19871201	FI 1987-2406	19870529
FI 90770	B	19931215		
FI 90770	C	19940325		
AU 8773684	A1	19871203	AU 1987-73684	19870529
AU 597982	B2	19900614		
JP 62289570	A2	19871216	JP 1987-134772	19870529
JP 07051571	B4	19950605		
HU 45978	A2	19880928	HU 1987-2487	19870529
HU 196769	B	19890130		
ZA 8703896	A	19890125	ZA 1987-3896	19870529
US 4847249	A	19890711	US 1987-56136	19870529
AT 62902	E	19910515	AT 1987-304776	19870529
CA 1286670	A1	19910723	CA 1987-538395	19870529
IL 82710	A1	19920115	IL 1987-82710	19870529
PRIORITY APPLN. INFO.:			GB 1986-13183	A 19860530
			EP 1987-304776	A 19870529

IT **84057-84-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and conversion of, into isethionate salt)

RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



IT **113170-86-8P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of, as anticonvulsant)

RN 113170-86-8 CAPLUS

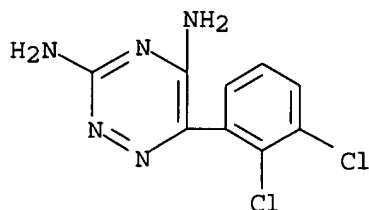
CN Ethanesulfonic acid, 2-hydroxy-, compd. with 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine (1:1) (9CI) (CA INDEX NAME)

10/532,397

CM 1

CRN 84057-84-1

CMF C9 H7 Cl2 N5



CM 2

CRN 107-36-8

CMF C2 H6 O4 S

HO-CH<sub>2</sub>-CH<sub>2</sub>-SO<sub>3</sub>H

AB The title compound (I.isethionate), useful as an anticonvulsant (no data), was **prepared** by reaction of I with 2-hydroxyethanesulfonic acid (II) or by reaction of I salts with the anion of II. A 1.0 M solution of Na isethionate in H<sub>2</sub>O was passed through a column of IR 120 (H) ion exchange resin. I (**preparation** given) was added to the resulting II and the solution was filtered and evaporated Recrystn. from industrial methylated spirit gave 72% I.isethionate.

L6 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:208914 CAPLUS

DOCUMENT NUMBER: 94:208914

TITLE: 1,2,4-Triazine derivatives, pharmaceutical compositions and intermediates utilized for their **preparation**

INVENTOR(S): Baxter, Martin George; Elphick, Albert Reginald; Miller, Alistair Ainslie; Sawyer, David Alan

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK

SOURCE: Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 21121	A1	19810107	EP 1980-103032	19800530
EP 21121	B1	19830511		
R: BE, CH, DE, FR, GB, LU, NL, SE				
DK 8002338	A	19801202	DK 1980-2338	19800530
DK 153787	B	19880905		
DK 153787	C	19890116		
FI 8001758	A	19801202	FI 1980-1758	19800530

FI 67844	B	19850228		
FI 67844	C	19850610		
AU 8058906	A1	19801204	AU 1980-58906	19800530
AU 530999	B2	19830804		
JP 56025169	A2	19810310	JP 1980-71580	19800530
JP 01044706	B4	19890929		
ES 491998	A1	19810516	ES 1980-491998	19800530
DD 151309	C	19811014	DD 1980-221474	19800530
ZA 8003250	A	19820127	ZA 1980-3250	19800530
AT 8002896	A	19820715	AT 1980-2896	19800530
AT 370097	B	19830225		
EP 59987	A1	19820915	EP 1982-102293	19800530
EP 59987	B1	19850814		

R: BE, CH, DE, FR, GB, LU, NL, SE

PL 124029	B1	19821231	PL 1980-224633	19800530
HU 24621	O	19830328	HU 1980-1364	19800530
HU 182086	B	19831228		
IL 60201	A1	19840531	IL 1980-60201	19800530
CS 234018	B2	19850314	CS 1980-3829	19800530
SU 1055331	A3	19831115	SU 1980-2932704	19800602
US 4486354	A	19841204	US 1981-308805	19811005
US 4602017	A	19860722	US 1984-583286	19840227
FI 8400888	A	19840306	FI 1984-888	19840306
FI 73203	B	19870529		
FI 73203	C	19870910		
JP 61033163	A2	19860217	JP 1985-121370	19850604
JP 01044179	B4	19890926		

PRIORITY APPLN. INFO.:

GB 1979-19257	A	19790601
US 1980-154198	A1	19800529
EP 1980-103032	A	19800530
FI 1980-1758	A	19800530
US 1981-302365	A1	19810915

OTHER SOURCE(S): MARPAT 94:208914

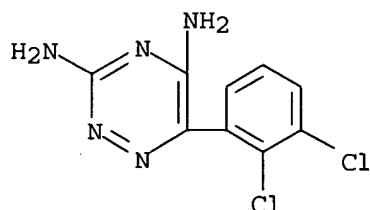
IT 84057-84-1P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);  
 SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation);  
 RACT (Reactant or reagent)

(preparation, acetylation and anticonvulsant activity of)

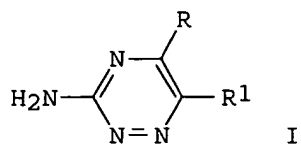
RN 84057-84-1 CAPLUS

CN 1,2,4-Triazine-3,5-diamine, 6-(2,3-dichlorophenyl)- (9CI) (CA INDEX NAME)



GI

10/532,397



AB    Triazines I (R = NH<sub>2</sub>, acylamino, aminomethyleneamino; R<sub>1</sub> = substituted Ph) were **prepared** Thus, 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>I was Grignard carboxylated and the 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub>H converted to the chloride and treated with CuCN to give 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>COCN which was cyclized with **aminoguanidine bicarbonate** to I (R = NH<sub>2</sub>, R<sub>1</sub> = 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>). The latter compound had an anticonvulsant ED<sub>50</sub> of 2.4 mg/kg orally in mice.

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

71.12

238.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.75

-6.75

STN INTERNATIONAL LOGOFF AT 16:43:41 ON 18 MAY 2006